Asthma, Chronic Bronchitis and Emphysema

The Use of Intermittent Positive Pressure Breathing with Inspiratory Flow Rate Control

A Review of the Literature

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• **In chronic obstructive lung disease (asthma, chronic bronchitis, obstructive emphysema) there is a segmental reduction in the caliber of the airways, which always results in obstruction to air-flow. Increased airway resistance is a physiological expression of airway obstruction.**

The addition of inspiratory flow rate control to an intermittent positive pressure breathing device permits slow filling of a lung with obstructed airways, and is presented as a simple means of reducing the high pulmonary flow resistance and increasing the tidal volume.

BRONCHIAL ASTHMA, chronic bronchitis and obstructive emphysema are disorders characterized by a segmental reduction in the caliber of the airways, which may be due to mucus, edema, inflammation, bronchiolar collapse, spasm or a combination of these phenomena.* While etiologically different, those disorders share a final common path of morphological expression—obstruction to airflow. This results in an increased airway resistance with subsequent impairment of pulmonary function. The most effective therapy, therefore, will include measures to relieve the airway obstruction and means to reduce the high flow resistance.

It is the purpose of this paper to briefly review the possible relationships between asthma, bronchitis and emphysema as chronic obstructive lung disorders, to consider how generalized airway obstruction always results in increased airway resistance, to outline the clinical effects of such an increase in resistance and to examine how the addition of an inspiratory flow rate control to a pressure breathing device may be of therapeutic value in directly lowering the high flow resistance.

The Importance of Generalized Airway Obstruction

A relationship may exist between asthma, bronchitis and emphysema such as is outlined in Chart 1.[34] It must be stressed at the outset that in many cases of asthma, chronic bronchitis never develops. Persons with mild asthma do not have significant airway obstruction. Consequently chronic infection rarely develops in them, and their disease, which is generally of the extrinsic or seasonal variety, does not go on to emphysema. Similarly, most cases of chronic bronchitis occur in persons who are not asthmatic, and there are patients with full blown emphysema who have no history of asthma or chronic bronchitis or any respiratory infection.

Presented in part at the Sixth International Congress of Diseases of the Chest in Vienna, September 1960.

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Submitted March 19, 1962.

*Reference Nos.: 3, 7, 22, 23, 26, 42, 45, 50, 54.

However, the high incidence of bronchitis and later emphysema in persons with chronic asthma,[40,50] and the almost constant association of unspecified chronic bronchitis with emphysema[19,56] are such that these occurrences must be more than fortuitous. *Severe asthma* leads to decided airway obstruction with ventilatory impairment whether it is etiologically traceable to an allergen or not. Chronic plugging of the distal airways with thick mucoid secretions predisposes to the development and maintenance of repeated infections. The infective factor is the dominant cause of 40 per cent of asthma in England and Canada.[52]

Bronchial asthma and asthmatic bronchitis are true causes of emphysema but not the sole ones.[19,45,50] The incidence of emphysema in patients with long standing asthma is increasing[40,50] and asthmatic patients with cor pulmonale who die in status asthmaticus show evidence of permanent bronchiolar damage and destructive emphysema.[53] If asthma is uncomplicated by episodes of infective bronchiolitis, destructive emphysema is not likely to occur, even if death is due to status asthmaticus.[17,53] In such cases the lungs only show hyperinflation, as those of a person who has drowned.[17] Pathologists are not unanimous in the histological definition of destructive emphysema at the bronchiolar level, and what is called emphysema by some may well be simple hyperinflation to others. Severely asthmatic children, following a period of intensive therapy, showed no signs of emphysema.[47] But in a 40-year survey of causes of death in asthmatic per-

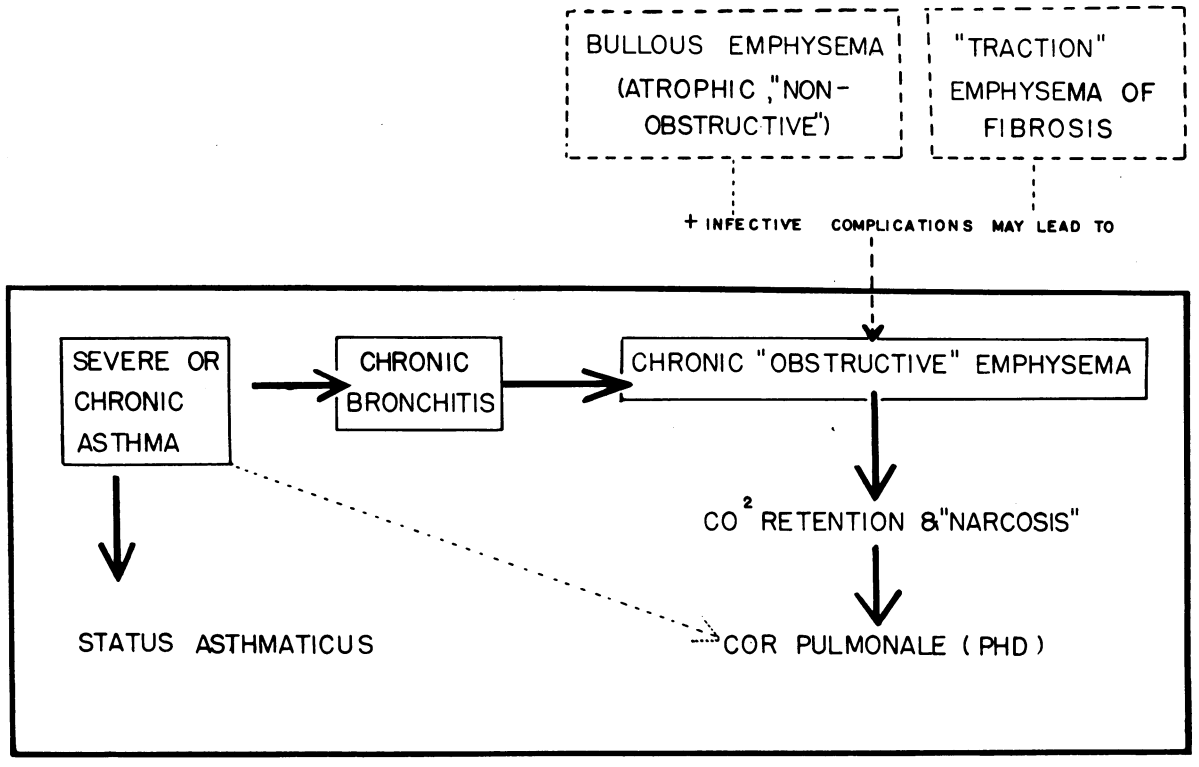

Chart 1.—The diseases of generalized airway obstruction. The chart shows the relationship that may exist between asthma, bronchitis and emphysema. (Adapted in part from Richards.[34])

sons conducted at the Mayo Clinic, all of the 35 patients who died in status asthmaticus and the 31 who died from the complications of asthma showed microscopic evidence of emphysema.[30]

Chronic bronchitis is the fourth ranking cause of death in Great Britain, where the mortality due to that disease is 45 times that recorded in this country.[13,16] Such a disparity may be due to particular conditions of climate and air pollution prevailing in England, but perhaps also to differences in diagnostic terminology.[13] Chronic bronchitis is not generally a consultant's diagnosis in the United States, where deaths due to that disease are more likely to be recorded as emphysema or pneumonia or, if right heart failure supervenes, as "arteriosclerotic or degenerative heart disease."

Emphysema is a complication and almost constant associate of chronic bronchitis, but it is found in other pulmonary conditions and therefore cannot be regarded solely as complication of chronic bronchitis.[45] However, patients with bronchitis who develop pulmonary heart disease and cor pulmonale uniformly show evidence of emphysema with widespread bronchiolar damage. Gaensler and Lindgen studied 555 cases of emphysema in Boston and found a definite history of chronic bronchitis in 68 per cent,[16] thus confirming that disorder as the commonest predisposing condition to emphysema.[44] It is also a widely held opinion that chronic bronchitis and emphysema are related by way of the common factor of inflammatory disease of the bronchioles.[24,27,32]

Chronic bronchitis is difficult to differentiate from asthma in middle aged men in whom paroxysmal dyspnea occurs for the first time.[45] Most cases of bronchitis do not develop in asthmatic subjects, but bronchospasm often occurs in moderately advanced chronic bronchitis, particularly on effort and during infective exacerbations. A prevalent definition of asthma in England is "reversible bronchial obstruction associated with chronic bronchitis."[13] Both chronic asthma and chronic bronchitis, with their partial airway obstruction, are associated with an increased susceptibility to recurrent bronchial infection, and hence possible bronchiolar damage with destructive emphysema.

Emphysema, lastly, is a term referring to both a syndrome and a group of disorders which may result in an irreversible distention of the air spaces with destruction of the lung parenchyma, where obstruction to airflow is usually a prominent morphological defect, and for which no unified pathogenesis has as yet been found. Emphysema is a disorder generally on the increase, with mortality rates having nearly doubled in this country between 1955 and 1958. In a recent discussion on the eti-

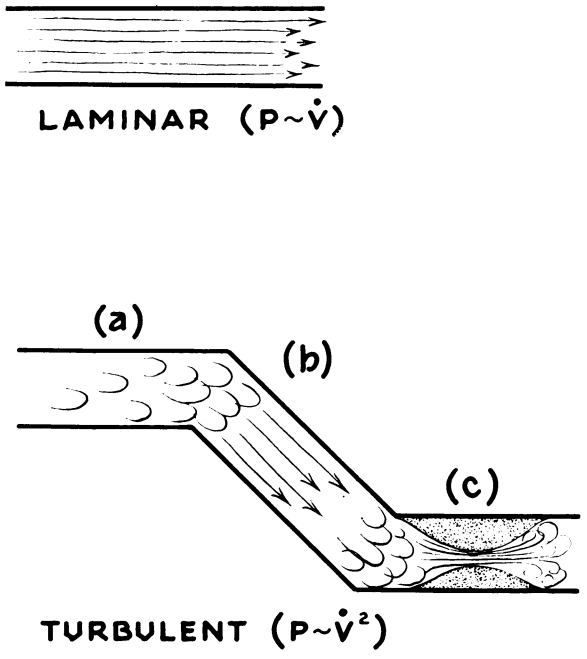

Chart 2.—The nature of airflow (adapted from Comroe[5]). Turbulence occurs when (a) flow is straight but at high velocity or (b) through a change in direction of the tube, or (c) through a narrowing of the tube.

ologic factors of emphysema, Richards made clear distinction between obstructive emphysema as a sequela of bronchitis, "traction" emphysema secondary to interstitial fibrosis as seen in coal miners' pneumonoconiosis, and "bullous emphysema," primarily nonobstructive and atrophic, viewed as a separate disease. In the last two forms, diffuse emphysema may, in time, develop, with true obstruction and secondary infection difficult to distinguish from those seen in bronchitis with emphysema.[34]

Most cases seen in clinical practice will be diffuse chronic obstructive emphysema with unspecified chronic bronchitis as a constant feature. It is this form of pulmonary emphysema which may progress more readily to pulmonary heart disease, as the obstruction worsens, the infective episodes recur and as the destruction of lung parenchyma and loss of vascular bed contribute slowly to a permanent state of hypoxia. In such cases cor pulmonale becomes well established, and right ventricular failure is the usual terminal event. The growing importance of pulmonary heart disease as a cause of congestive failure remains generally underestimated.[32] It is the obstructive form of emphysema also which benefits most from measures designed to relieve the obstruction and to reduce the high flow resistance.

Thus, irrespective of differences in their etiologic delineation, asthma, chronic bronchitis and emphysema maintain a certain relationship which centers on obstruction to airflow. Essentially, this relationship suggests that bronchiolar obstruction with infection may play a significant part in the development of diffuse chronic obstructive emphysema but not in the other forms of that disease. For these reasons, the vigorous treatment and effective prophylaxis of early and latent forms of generalized airway obstruction assumes a new importance.

Increased Airway Resistance

The main physiological aberration resulting from obstruction to airflow is increased airway resistance. This fact has been documented by extensive investigations.[10,11,15,25,28] In its simplest expression, airway resistance is a pressure flow relationship which measures the flow-resistive properties of the lung ($R \sim P/\dot{V}$), where the pressure, P, is the gradient required for flow and the flow, $\dot{V}$, is the volume per second.[5,8,14] Pressure depends on the dimensions of the airway and on the *work of breathing*. Flow depends also on the dimensions of the airways and on the *mechanics of airflow*.

The work of breathing generates the pressure gradient required for airflow and is the sum of elastic work to overcome elastic resistance in the lungs and thorax, plus resistive work to overcome airway resistance. The former is expressed as a pressure-volume relationship, or compliance; the latter as a pressure-flow relationship, or resistance.[5,8,14]

The mechanics of airflow determine largely the variations in the nature and rate of airflow observed from changing conditions in the airways. The laws of hydraulics which govern the friction of flowing fluids, and which were defined by Poiseuille for the flow of liquids through very small tubes,[33] may apply to air flowing through tubes.[5,36] These laws define *laminar* flow as streamlined and *turbulent* flow as that in which there are disturbed conditions in the flowing fluid. Chart 2, adapted from Comroe,[5] shows that turbulence occurs when air flows through a straight tube at high velocity or through irregular branching tubes or through narrow obstructed airways.

Rohrer pointed out that these same laws determine also the *rate* at which air flows through tubes.[36] He showed that the pressure required for laminar flow varies roughly as the velocity ($P \sim \dot{V}$) while the pressure for turbulent flow varies as the square of the velocity ($P \sim \dot{V}^2$). Tracheobronchial flow, on the other hand, is a composite of both laminar and turbulent flow.[5,36] Depending upon the dimensions of the airway, flow will be more laminar or more turbulent, and when the smallest air passages become partially obstructed, turbulence develops.[12] Therefore, in generalized obstructive airway disease, the pressure-flow relationship within the lung is decid-

edly altered because of a reduction in the airway's cross-sectional area due to bronchiolar collapse, mucosal edema, spasm inflammation, or a combination of these factors. *This reduction in the dimensions of the airways modifies both the pressure required for flow and the nature of airflow.*[5,11] Thus, narrowing and obstruction of the airways promote a greater degree of turbulence[12] and the pressure required to sustain turbulent flow will vary as the square of the velocity. Consequently, with an increase in turbulence, both pressure and flow increase, and airway resistance—which is a pressure-flow relationship—also rises.[39]

In summary, an increase in airway resistance is observed in any case of generalized airway obstruction and is responsible for the pronounced increase in the "resistive" work of breathing so characteristic of patients with severe asthma and emphysema.[15] Airway resistance, then, is a useful index of the flow resistive properties of the lung and of airway obstruction in general. Airway resistance depends essentially on the dimensions of the airways—which determine the pressure required for flow, and on the nature and rate of airflow. But it also varies with different degrees of lung inflation[14] and with the rate at which the lungs are changing volume.[28] According to Mead and coworkers[28] this explains why, in patients with emphysema, rapid breathing does not permit diseased areas of the lung to empty well during expiration, thus causing a drop in compliance in addition to the increased airway resistance.[28]

Effects of Sustained Increased Airway Resistance on Pulmonary Function

Increased airway resistance is a constant physiological defect in asthma, chronic bronchitis and obstructive emphysema, and it is present throughout the entire course of those disorders. Since it measures accurately the flow resistive properties of the lung, it is a convenient quantitative index of airway obstruction, and its effects on pulmonary function are those of generalized obstructive airway disease.

The main function of the lung is gas exchange. For diffusion to take place across a normal alveolo-capillary membrane, ventilation must lead to even distribution of inspired air on one side of that membrane, and pulmonary circulation must provide even capillary distribution on the other side. The three main components of pulmonary function are therefore *ventilation*, which is mostly mechanical, *diffusion*, which is physico-chemical, and *transport* of gases in the blood, which is circulatory. The first effect of increased airway resistance is a reduction in minute ventilation.[2] If more time is not available for adequate tidal respiration, the functional residual volume increases. This may alter the compliance of the lung[36] and will increase its flow resistive properties.[29] As a result the work of breathing increases to overcome the added pulmonary flow resistance, and dyspnea on exertion is the first manifestation of increased airway resistance.[35] In this first phase of pulmonary insufficiency, the major disability is reduction in the breathing reserve, which limits physical activity; but there is usually no significant hypoxia because the chest bellows can still compensate through hyperventilation.[6,51]

As increased airway resistance is maintained for prolonged periods, its effects become more severe, and alveolar hypoventilation occurs. Ineffective gas exchange of varying degrees of severity compounds the ventilatory insufficiency, carbon dioxide is retained, hypoxia develops, and, at the end of this sequence, respiratory acidosis.[4,41] This at first can be reversed with adequate therapy, but in the more advanced stages of the disease it may become a permanent chronic defect.[6,51] This, then, is the second phase of pulmonary insufficiency.

With the progression of emphysema into its advanced stages, the effects of increased airway resistance become still more pronounced and may lead to the development of pulmonary heart disease. The factors responsible for the development of that disorder are still not fully known. However, as hypoxia and further destruction of pulmonary parenchyma seem to go hand in hand in the later stages of emphysema, there is also a loss of vascular bed and a decided increase in resistance to pulmonary blood flow.[51] These are the factors which are believed to contribute to the development of pulmonary hypertension, the forerunner of pulmonary heart disease. Evidence of right ventricular hypertrophy is then common, as are constant disturbances in the ventilation-perfusion relationship.[34] In such circumstances, if for any reason alveolar hypoventilation with hypercapnia and hypoxia become aggravated, an exacerbation of pulmonary hypertension is likely to occur and may result in acute right heart failure, or early cor pulmonale. This is characterized by cardiac enlargement, elevated venous pressure, cyanosis, hepatomegaly and edema.[9]

With adequate treatment, the acute bronchopulmonary infection resolves, airway obstruction is relieved, hypoxia improves and heart failure subsides. The same picture of cardiopulmonary failure may recur with each serious exacerbation of the primary disorder, which triggers off episodes of alveolar hypoventilation. However, in the last stages of the disease, right heart failure and cor pulmonale may become chronic, and as each acute episode is more difficult to treat, death may then be due to both ventilatory and congestive heart failure.[1,6,35,51] As was pointed out earlier, the importance of pul-

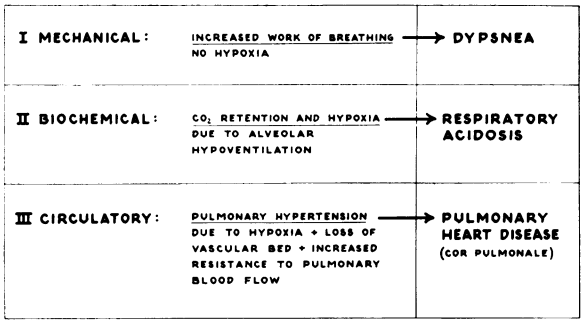

Chart 3.—Effects of prolonged increase in airway resistance on pulmonary function.

monary heart disease as a cause of heart failure is still grossly underestimated.[1,32,51] The effects of prolonged increases in airway resistance on pulmonary function are those that are observed in the natural course of chronic obstructive lung disease with pulmonary emphysema.[9] (See Chart 3.)

Direct Reduction in Airway Resistance in the Management of Asthma, Chronic Bronchitis and Emphysema

As has been noted, airway resistance is primarily a function of the rate of flow.[5,10,11,15,28] Obstructed or narrowed airways predispose to turbulent flow, and high rates of inspiratory flow tend to increase the turbulence. As the pressure required for turbulent flow is large, the airway resistance and the work to overcome it both increase in an attempt to maintain sufficient pressure for adequate flow. If the obstruction becomes more severe, and the flow still more turbulent, a point is reached at which further increase in pressure causes no further increase in flow, and volume flow falls.[7,11,15,28] In such cases, a decrease in the velocity of the inspired gas will best lower the airway resistance and permit flow to occur.

Reduction in high pulmonary flow resistance plays therefore a prominent part in the management of chronic obstructive lung disorders. In this connection, intermittent positive pressure breathing (IPPB) is an effective aid to bronchodilation and reduces the work of breathing.[37,38] However, respirators for IPPB used in the majority of hospitals today, while producing a type III curve,[31]* do not permit inspiratory flow rate control independently of pressure settings, and are therefore ineffective in *directly* reducing the high flow resistance encountered in severe obstructive lung disease. The reasons for failure of IPPB to improve alveolar ventilation in patients with severest emphysema in acute respiratory failure were studied by Jones, McNamara and Gaensler.[20] They showed that high inspiratory pressure is a frequent cause of poor result with IPPB, and that in severely ill patients with advanced airway obstruction and borderline heart failure, pressure breathing at times "may be physiologically and psychologically unbearable."[20] But these investigators did not study the effects of inspiratory flow rate control on obstructed breathing, since they used a conventional respirator with fixed high inspiratory flow rate, which did not permit individual flow rate adjustment.

Fixed high inspiratory flow rates delivered by most conventional machines are those of the unmetered line pressure and attempt to fill the lung rapidly. However, rapid delivery of inspired gases to an obstructed airway (as is the case with all respirators for IPPB without flow rate control) increases the eddying turbulence, hence increases the pressure to sustain flow and thus increases the airway resistance in that particular airway. This adds to the high flow resistance due to the obstructive disease itself, and causes the cycling pressure of the IPPB machine to be reached early in inspiration, leaving the patient literally short of breath, since passive lung insufflation stops before all of the distal airspaces become filled—that is, before the end of a complete inspiration. This explains why, in a severely obstructed airway, "peak machine flow is insufficient for inspiration."[20] By the same token, bronchodilators in the inspired gases tend to precipitate in the eddying turbulence generated in the upper airway, and cannot be carried distally where they are needed most. When this occurs, the patient desperately struggles for air. This further increases the work of breathing, which aggravates both the hypoxia and the alveolar hypoventilation and results in additional burden on the circulation. If the IPPB pressure is then suddenly increased, this will add to the gravity of the situation and may be injurious to a perhaps failing heart.[50] For these reasons, rapid mechanical lung filling in patients with severe obstructive airway disease and borderline heart failure, may have serious effects on both the ventilation and the circulation.

If, on the other hand, the IPPB machine used permits independent adjustment of the inspiratory flow rates to the particular degree of patency of an individual patient's airways, *slow* and more complete filling of that patient's lung becomes possible with each passive inspiration. In the presence of segmental airway obstruction, as occurs in chronic bronchitis, bronchial asthma and obstructive emphysema, what is needed is not that the IPPB respirator reach a peak flow, which may cycle the machine before inspiration is complete, but that the respirator be adjusted to maintain a slow but sustained flow to the distal airspaces. Slow flow rates will minimize eddying turbulence, diminish the pressure

*Type III curve is the only mask pressure curve which will not engender circulatory ill effects (as was the case with earlier respirators which produced Type I and Type II curves).[31]

IPPB WITH HIGH FLOW-RATE	IPPB WITH LOW FLOW-RATE
1. ↑ IN EDDYING TURBULENCE (RAPID LUNG FILLING)	1. ↓ IN EDDYING TURBULENCE (SLOW LUNG FILLING)
2. ↑ IN PRESSURE TO MAINTAIN FLOW ($\dot{V} \rightarrow \dot{V}^2$)	2. ↓ IN PRESSURE NEEDED FOR FLOW ($\dot{V}^2 \rightarrow \dot{V}$)
3. ↑ IN AIRWAY RESISTANCE (R=P/$\dot{V}$)	3. ↓ IN AIRWAY RESISTANCE.
4. CYCLING PRESSURE REACHED EARLY IN INSPIRATION. LUNGS STOP FILLING BEFORE DISTAL OBSTRUCTED AIRWAYS BECOME VENTILATED.	4. CYCLING PRESSURE REACHED LATE. LUNGS KEEP ON FILLING SLOWLY UNTIL ALL AIRSPACES BECOME VENTILATED.
	∴ A. COMPLIANCE ↑ (LUNG "STIFFNESS" ↓)
	B. TIDAL VOLUME INCREASES.
	C. MORE EVEN LUNG FILLING.
	D. IMPROVED INTRAPULMONARY GAS MIXING.

Chart 4.—Effects of intermittent positive pressure breathing with high and low inspiratory flow rate on obstructed breathing.

required for flow, reduce the airway resistance and permit the cycling pressure to be reached late in a passive inspiration, because the intra-airway pressure rises *slowly* as the lungs gradually comply with increasing inspiratory volumes.[39] It must be stressed that since the pressure rises gradually, the machine cycling is delayed, giving time to the lung to fill slowly but more completely. This results in increased tidal volumes, permits more even lung filling, improves intrapulmonary gas mixing[49] and does not lead to sudden pressure increases, which may be harmful to an impaired circulation. The effects of IPPB with high and low inspiratory flow rates on patients with severe airway obstruction are summarized in Chart 4.

Sieker and Hickam were among the first to point out that a respirator which delivered gas at slow flow rates permitted greater tidal volume and a more even gas distribution throughout the lung of a patient with high airway resistance than was the case when the gas was delivered rapidly.[41] In view of the importance of slow filling of the lung in the reduction of high airway resistance,[15,28] a portable device for the production of intermittent positive pressure breathing—the Mark VII which could control the rate of flow of inspired gases independently of the pressure at which the respirator was set—was designed in 1957 by Bird. This was made possible through metering of the line pressure so that the inspired gases could be given sufficient time to pass through narrowed or collapsed bronchioles.[39] The main advantage of such a device is that inspiratory flow rates can be adjusted to suit the patient's individual needs. Adjustable flow rates of the inspired gases had been recommended in IPPB devices as early as 1948[31] but did not become generally available until a decade later.[39] It is of considerable therapeutic significance that slow filling of the lung in the presence of widespread airway obstruction directly reduces the eddying turbulence largely responsible for the high flow resistance, and hence reduces the resistance.[39] Such a diminution in airway resistance leads to increase in both compliance and tidal volume and to a reduction in the work of breathing.[37] This permits also more even lung filling[49] and results in improved capillary perfusion because of a relaxation in arteriolar spasm[18] and in more effective intrapulmonary gas mixing.[48,49]

In this regard, artificial ventilation experiments were conducted on fresh lungs taken in the postmortem state from patients with airway obstruction.

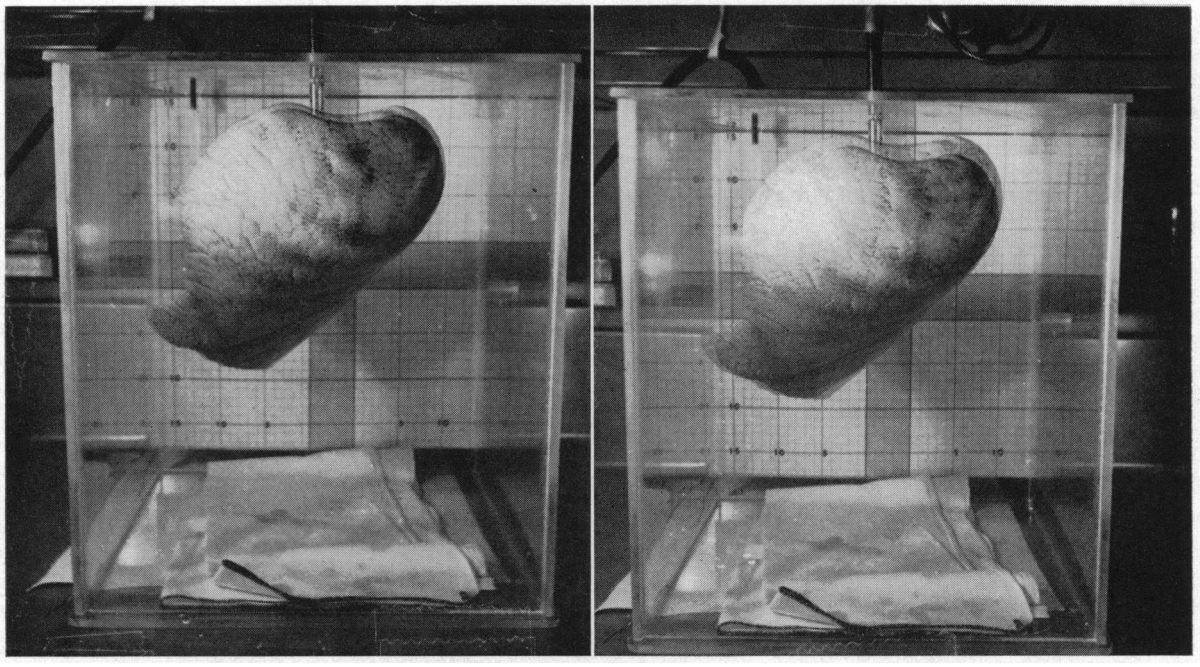

Figure 1.—Superimposed photographs, taken at 1/250 second, of inspiration and expiration in a slightly emphysematous lung "ventilated" by a Mark VII respirator (not shown in picture) set on automatic breathing rate. *At left,* with no inspiratory flow rate control, the respiratory excursions are less than those observed at right, where the rate of flow of inspired gases has been adjusted to the particular needs of the lung's airways, independently of the pressure limit at which the respirator is set (12 cm., water). The plastic cage shown simulates a human thorax. Continuous suction maintains a negative pressure of −6 cm. of water to avoid expiratory collapse. The amplitude of the respiratory excursions may be taken as a rough index of the tidal volume.

These lungs were set up in a plastic cage simulating the human thorax and connected to an IPPB respirator which could be set at different automatic breathing rates, different inspiratory pressures and different inspiratory flow rates. Figure 1 shows the amplitude of the respiratory excursions during the artificial ventilation of a lung with airway obstruction, and demonstrates simply that in the presence of airway obstruction slow inspiratory filling permits greater respiratory excursions than is obtained with fast filling.[39] The amplitude of these excursions may be taken as a rough index of the lung's tidal volume.

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